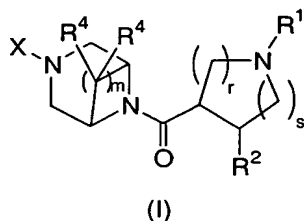


WHAT IS CLAIMED IS:

1. A compound of structural formula I:



- 5 or a pharmaceutically acceptable salt thereof;
wherein

X is selected from the group consisting of

- | | | |
|----|------|--|
| | (1) | C ₁₋₈ alkyl, |
| 10 | (2) | -(CH ₂) _n C ₃₋₈ cycloalkyl, |
| | (3) | -(CH ₂) _n -phenyl, |
| | (4) | -(CH ₂) _n -naphthyl, |
| | (5) | -(CH ₂) _n -heteroaryl, |
| | (6) | -(CH ₂) _n heterocycloalkyl, |
| 15 | (7) | -(CH ₂) _n C(R ⁵)(R ⁶)(R ⁷), |
| | (8) | -(CH ₂) _n C≡N, |
| | (9) | -(CH ₂) _n CON(R ⁸) ₂ , |
| | (10) | -(CH ₂) _n CO ₂ R ⁸ , |
| | (11) | -(CH ₂) _n COR ⁸ , |
| 20 | (12) | -(CH ₂) _n NR ⁸ C(O)R ⁸ , |
| | (13) | -(CH ₂) _n NR ⁸ CO ₂ R ⁸ , |
| | (14) | -(CH ₂) _n NR ⁸ C(O)N(R ⁸) ₂ , |
| | (15) | -(CH ₂) _n NR ⁸ SO ₂ R ⁸ , |
| | (16) | -(CH ₂) _n S(O) _p R ⁸ , |
| 25 | (17) | -(CH ₂) _n SO ₂ N(R ⁸) ₂ , |
| | (18) | -(CH ₂) _n OR ⁸ , |
| | (19) | -(CH ₂) _n OC(O)R ⁸ , |
| | (20) | -(CH ₂) _n OC(O)OR ⁸ , |
| | (21) | -(CH ₂) _n OC(O)N(R ⁸) ₂ , |
| 30 | (22) | -(CH ₂) _n N(R ⁸) ₂ , and |



wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3 , and alkyl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted with one to three groups independently selected from R^3 and oxo, and wherein any methylene (CH_2) in X is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C_{1-4} alkyl;

R^1 is selected from the group consisting of

- (1) hydrogen,
- (2) amidino,
- (3) C_{1-4} alkyliminoyl,
- (4) C_{1-10} alkyl,
- (5) $-(\text{CH}_2)_n\text{-C}_{3-7}$ cycloalkyl,
- (6) $-(\text{CH}_2)_n\text{-phenyl}$,
- (7) $-(\text{CH}_2)_n\text{-naphthyl}$, and
- (8) $-(\text{CH}_2)_n\text{-heteroaryl}$,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3 , and alkyl and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from R^3 and oxo;

R^2 is selected from the group consisting of

- (1) phenyl,
- (2) naphthyl, and
- (3) heteroaryl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3 ;

each R^3 is independently selected from the group consisting of

- (1) C_{1-8} alkyl,
- (2) C_{2-8} alkenyl,
- (3) $-(\text{CH}_2)_n\text{-phenyl}$,
- (4) $-(\text{CH}_2)_n\text{-naphthyl}$,
- (5) $-(\text{CH}_2)_n\text{-heteroaryl}$,
- (6) $-(\text{CH}_2)_n\text{C}_{2-7}$ heterocycloalkyl,
- (7) $-(\text{CH}_2)_n\text{C}_{3-7}$ cycloalkyl,

- (8) halogen,
 (9) OR⁹,
 (10) -(CH₂)_nC(O)R⁹,
 (11) -(CH₂)_nOC(O)R⁹,
 5 (12) -(CH₂)_nC(O)OR⁹,
 (13) -(CH₂)_nC≡N,
 (14) NO₂,
 (15) -(CH₂)_nN(R⁹)₂,
 (16) -(CH₂)_nC(O)N(R⁹)₂,
 10 (17) -(CH₂)_nNR⁹C(O)R⁹,
 (18) -(CH₂)_nNR⁹C(O)OR⁹,
 (19) -(CH₂)_nNR⁹C(O)-heteroaryl,
 (20) -(CH₂)_nNR⁹C(O)N(R⁹)₂,
 (21) -(CH₂)_nC(O)NR⁹N(R⁹)₂,
 15 (22) -(CH₂)_nC(O)NR⁹NR⁹C(O)R⁹,
 (23) -(CH₂)_nNR⁹S(O)_pR⁹,
 (24) -(CH₂)_nS(O)_pN(R⁹)₂,
 (25) -(CH₂)_nS(O)_pR⁹,
 (26) O(CH₂)_nC(O)N(R⁹)₂,
 20 (27) CF₃,
 (28) CH₂CF₃,
 (29) OCF₃, and
 (30) OCH₂CF₃,

wherein alkenyl, phenyl, naphthyl, heteroaryl are unsubstituted or substituted with one to three
 25 substituents independently selected from halogen, hydroxy, C₁₋₄ alkyl, trifluoromethyl, and C₁₋₄
 alkoxy, and wherein any alkyl, cycloalkyl, heterocycloalkyl, and methylene (CH₂) carbon atom
 in R³ is unsubstituted or substituted with one to two groups independently selected from
 halogen, hydroxy, oxo, C₁₋₄ alkyl, trifluoromethyl, and C₁₋₄ alkoxy, or two R³ substituents on
 the same carbon atom are taken together with the carbon atom to form a cyclopropyl group;

30

each R⁴ is independently selected from the group consisting of

- (1) hydrogen,
 (2) C₁₋₈ alkyl,
 (3) -(CH₂)_nC₃₋₆ cycloalkyl,
 35 (4) -(CH₂)_n-aryl,

- (5) hydroxy,
- (6) halogen, and
- (7) amino;

5 R^5 is independently selected from the group consisting of

- (1) hydrogen,
- (2) C_{1-8} alkyl,
- (3) C_{2-8} alkenyl,
- (4) C_{2-8} alkynyl,
- 10 (5) C_{1-8} alkoxy,
- (6) $-(CH_2)_n C_{3-7}$ cycloalkyl,
- (7) $-(CH_2)_n C_{2-7}$ heterocycloalkyl,
- (8) $-(CH_2)_n$ -phenyl,
- (9) $-(CH_2)_n$ -naphthyl,
- 15 (10) $-(CH_2)_n$ -heteroaryl, and
- (11) $-(CH_2)_n C_{3-7}$ bicycloalkyl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3 , and alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups
 20 independently selected from R^3 and oxo, and wherein any methylene (CH_2) in R^5 is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C_{1-4} alkyl;

R^6 is selected from the group consisting of

- 25 (1) hydrogen, and
- (2) C_{1-8} alkyl;

R^7 is selected from the group consisting of

- (1) $-(CH_2)_n N(R^8)_2$,
- 30 (2) $-(CH_2)_n NR^8 C(O)R^8$,
- (3) $-(CH_2)_n NR^8 C(O)OR^8$,
- (4) $-(CH_2)_n NR^8 C(O)N(R^8)_2$,
- (5) $-(CH_2)_n NR^8 S(O)R^8$,
- (6) $-(CH_2)_n NR^8 S(O)_2 R^8$, and
- 35 (7) $-(CH_2)_n NR^8 S(O)_2 N(R^8)_2$,

wherein any methylene (CH₂) in R⁷ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl, or two R⁸ substituents together with the carbon, nitrogen or sulfur atom to which they are attached form a 5, 6, or 7-membered saturated or unsaturated nitrogen containing ring optionally substituted with one to three groups independently selected from C₁₋₈ alkyl and oxo;

each R⁸ is independently selected from the group consisting of

- (1) hydrogen,
- (2) C₁₋₈ alkyl,
- (3) C₂₋₈ alkenyl,
- (4) -(CH₂)_nC₃₋₇ cycloalkyl,
- (5) -(CH₂)_nC₂₋₇ heterocycloalkyl,
- (6) -(CH₂)_nC₃₋₇ bicycloalkyl,
- (7) -(CH₂)_n-phenyl,
- (8) -(CH₂)_n-naphthyl, and
- (9) -(CH₂)_n-heteroaryl,

wherein alkyl, alkenyl, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from R³ and oxo, and wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R³, and wherein any methylene (CH₂) in R⁸ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl, or two R⁸ groups together with the atom to which they are attached form a 5- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC₁₋₄ alkyl;

each R⁹ is independently selected from the group consisting of

- (1) hydrogen,
- (2) C₁₋₈ alkyl,
- (3) phenyl,
- (4) heteroaryl,
- (5) -(CH₂)_n heterocycloalkyl, and
- (6) C₃₋₆ cycloalkyl,

wherein alkyl, phenyl, heteroaryl, heterocycloalkyl, and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from halogen, C₁₋₄ alkyl, hydroxy,

and C₁₋₄ alkoxy, or two R⁹ groups together with the atom to which they are attached form a 4- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC₁₋₄ alkyl;

r is 1 or 2;

5 s is 0, 1, or 2;

m is 0, 1, 2, 3, or 4;

n is 0, 1, 2, 3, or 4; and

p is 0, 1, or 2.

10 2. The compound of Claim 1 wherein R¹ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, -(CH₂)₀₋₁C₃₋₆ cycloalkyl, and -(CH₂)₀₋₁-phenyl, wherein phenyl is unsubstituted or substituted with one to three groups independently selected from R³, and alkyl and cycloalkyl are optionally substituted with one to three groups independently selected from R³ and oxo; and pharmaceutically acceptable salts
15 thereof.

3. The compound of Claim 1 wherein R² is phenyl or thienyl, optionally substituted with one to three groups independently selected from R³; and pharmaceutically acceptable salts thereof.

20 4. The compound of Claim 3 wherein R² is phenyl optionally substituted with one to three groups independently selected from R³; and pharmaceutically acceptable salts thereof.

25 5. The compound of Claim 1 wherein each R⁴ is independently selected from the group consisting of hydrogen, halogen, or hydroxy; and pharmaceutically acceptable salts thereof.

30 6. The compound of Claim 1 wherein X is selected from the group consisting of

- (1) C₁₋₈ alkyl,
- (2) -(CH₂)_nC₃₋₈ cycloalkyl,
- (3) -(CH₂)_n-phenyl,
- (4) -(CH₂)_n-heteroaryl,
- 35 (5) -(CH₂)_nheterocycloalkyl, and

(6) $-(\text{CH}_2)_n\text{C}(\text{R}^5)(\text{R}^6)(\text{R}^7)$,

wherein phenyl and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3 , and alkyl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted with one to three groups independently selected from R^3 and oxo, and wherein any methylene (CH_2) in X is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C_{1-4} alkyl; and pharmaceutically acceptable salts thereof.

7. The compound of Claim 6 wherein X is phenyl or heteroaryl optionally substituted with one to three groups independently selected from R^3 ; and pharmaceutically acceptable salts thereof.

8. The compound of Claim 7 wherein X is phenyl optionally substituted with one to three groups independently selected from R^3 ; and pharmaceutically acceptable salts thereof.

9. The compound of Claim 6 wherein X is $-(\text{CH}_2)_n\text{C}(\text{R}^5)(\text{R}^6)(\text{R}^7)$; and pharmaceutically acceptable salts thereof.

10. The compound of Claim 9 wherein
n is 0;
 R^5 is selected from the group consisting of

- (1) C_{1-8} alkyl,
- (2) $-(\text{CH}_2)_n\text{C}_{3-7}$ cycloalkyl,
- (3) $-(\text{CH}_2)_n\text{C}_{2-7}$ heterocycloalkyl,
- (4) $-(\text{CH}_2)_n$ -phenyl, and
- (5) $-(\text{CH}_2)_n$ -heteroaryl,

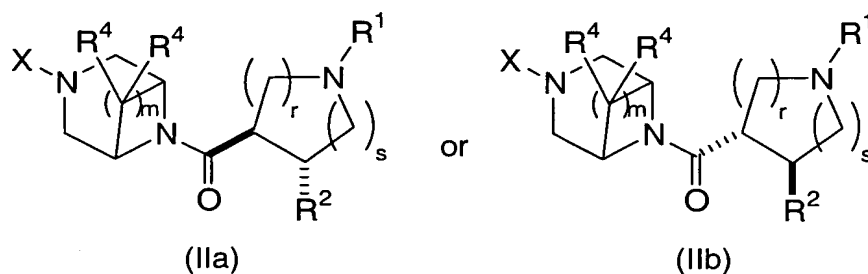
wherein phenyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3 , and alkyl, cycloalkyl and heterocycloalkyl are unsubstituted or substituted with one to three groups independently selected from R^3 and oxo, and wherein any methylene (CH_2) in R^5 is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C_{1-4} alkyl; and
 R^6 is hydrogen; and
pharmaceutically acceptable salts thereof.

11. The compound of Claim 1 wherein r is 1.

12. The compound of Claim 1 wherein r is 2.

13. The compound of Claim 1 wherein R^2 is phenyl substituted with one to three groups independently selected from R^3 .

14. The compound of Claim 1 of structural formula IIa or IIb of the indicated *trans* relative stereochemical configuration:



10 or a pharmaceutically acceptable salt thereof;
wherein

X is selected from the group consisting of

- (1) C_{1-8} alkyl,
- 15 (2) $-(CH_2)_n C_{3-8}$ cycloalkyl,
- (3) $-(CH_2)_n$ -phenyl,
- (4) $-(CH_2)_n$ -heteroaryl,
- (5) $-(CH_2)_n$ heterocycloalkyl, and
- (6) $-(CH_2)_n C(R^5)(R^6)(R^7)$,

20 wherein phenyl and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3 , and alkyl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted with one to three groups independently selected from R^3 and oxo, and wherein any methylene (CH_2) in X is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C_{1-4} alkyl;

25 R^1 is selected from the group consisting of hydrogen, amidino, C_{1-4} alkyliminoyl, C_{1-6} alkyl, C_{5-6} cycloalkyl, $-(CH_2)_{0-1}$ phenyl, and $-(CH_2)_{0-1}$ heteroaryl, wherein phenyl and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3 , and alkyl

and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from R³ and oxo;

R² is phenyl or thienyl, optionally substituted with one to three groups independently selected from R³;

each R³ is independently selected from the group consisting of

- (1) C₁₋₈ alkyl,
- (2) C₂₋₈ alkenyl,
- (3) -(CH₂)_n-phenyl,
- (4) -(CH₂)_n-naphthyl,
- (5) -(CH₂)_n-heteroaryl,
- (6) -(CH₂)_nC₂₋₇ heterocycloalkyl,
- (7) -(CH₂)_nC₃₋₇ cycloalkyl,
- (8) halogen,
- (9) OR⁹,
- (10) -(CH₂)_nC(O)R⁹,
- (11) -(CH₂)_nOC(O)R⁹,
- (12) -(CH₂)_nC(O)OR⁹,
- (13) -(CH₂)_nC≡N,
- (14) NO₂,
- (15) -(CH₂)_nN(R⁹)₂,
- (16) -(CH₂)_nC(O)N(R⁹)₂,
- (17) -(CH₂)_nNR⁹C(O)R⁹,
- (18) -(CH₂)_nNR⁹C(O)OR⁹,
- (19) -(CH₂)_nNR⁹C(O)-heteroaryl,
- (20) -(CH₂)_nNR⁹C(O)N(R⁹)₂,
- (21) -(CH₂)_nC(O)NR⁹N(R⁹)₂,
- (22) -(CH₂)_nC(O)NR⁹NR⁹C(O)R⁹,
- (23) -(CH₂)_nNR⁹S(O)_pR⁹,
- (24) -(CH₂)_nS(O)_pN(R⁹)₂,
- (25) -(CH₂)_nS(O)_pR⁹,
- (26) O(CH₂)_nC(O)N(R⁹)₂,
- (27) CF₃,
- (28) CH₂CF₃,

(29) OCF₃, and

(30) OCH₂CF₃,

wherein alkenyl, phenyl, naphthyl, heteroaryl are unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, C₁₋₄ alkyl, trifluoromethyl, and C₁₋₄ alkoxy, and wherein any alkyl, cycloalkyl, heterocycloalkyl, and methylene (CH₂) carbon atom in R³ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, oxo, C₁₋₄ alkyl, trifluoromethyl, and C₁₋₄ alkoxy, or two R³ substituents on the same carbon atom are taken together with the carbon atom to form a cyclopropyl group;

each R⁴ is independently selected from the group consisting of

- (1) hydrogen,
- (2) C₁₋₈ alkyl,
- (3) -(CH₂)₀₋₁C₃₋₆ cycloalkyl,
- (4) -(CH₂)₀₋₁-aryl,
- (5) hydroxy,
- (6) halogen, and
- (7) amino;

R⁵ is independently selected from the group consisting of

- (1) hydrogen,
- (2) C₁₋₈ alkyl,
- (3) C₂₋₈ alkenyl,
- (4) C₂₋₈ alkynyl,
- (5) C₁₋₈ alkoxy,
- (6) -(CH₂)_nC₃₋₇ cycloalkyl,
- (7) -(CH₂)_nC₂₋₇ heterocycloalkyl,
- (8) -(CH₂)_n-phenyl,
- (9) -(CH₂)_n-naphthyl,
- (10) -(CH₂)_n-heteroaryl, and
- (11) -(CH₂)_nC₃₋₇ bicycloalkyl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R³, and alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from R³ and oxo, and wherein any methylene (CH₂) in R⁵ is

unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl;

R⁶ is selected from the group consisting of

- 5 (1) hydrogen, and
- (2) C₁₋₈ alkyl;

R⁷ is selected from the group consisting of

- (1) -(CH₂)_nN(R⁸)₂,
- 10 (2) -(CH₂)_nNR⁸C(O)R⁸,
- (3) -(CH₂)_nNR⁸C(O)OR⁸,
- (4) -(CH₂)_nNR⁸C(O)N(R⁸)₂,
- (5) -(CH₂)_nNR⁸S(O)R⁸,
- (6) -(CH₂)_nNR⁸S(O)₂R⁸, and
- 15 (7) -(CH₂)_nNR⁸S(O)₂N(R⁸)₂,

wherein any methylene (CH₂) in R⁷ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl, or two R⁸ substituents together with the carbon, nitrogen or sulfur atom to which they are attached form a 5, 6, or 7-membered saturated or unsaturated nitrogen containing ring optionally substituted with one to three groups independently selected from C₁₋₈ alkyl and oxo;

each R⁸ is independently selected from the group consisting of

- (1) hydrogen,
- (2) C₁₋₈ alkyl,
- 25 (3) C₂₋₈ alkenyl,
- (4) -(CH₂)_nC₃₋₇ cycloalkyl,
- (5) -(CH₂)_nC₂₋₇ heterocycloalkyl,
- (6) -(CH₂)_nC₃₋₇ bicycloalkyl,
- (7) -(CH₂)_n-phenyl,
- 30 (8) -(CH₂)_n-naphthyl, and
- (9) -(CH₂)_n-heteroaryl,

wherein alkyl, alkenyl, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from R³ and oxo, and wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R³, and wherein any methylene (CH₂) in R⁸ is unsubstituted or

substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl, or two R⁸ groups together with the atom to which they are attached form a 5- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC₁₋₄ alkyl;

5

each R⁹ is independently selected from the group consisting of

- (1) hydrogen,
- (2) C₁₋₈ alkyl,
- (3) phenyl,
- 10 (4) heteroaryl,
- (5) -(CH₂)_n heterocycloalkyl, and
- (6) C₃₋₆ cycloalkyl,

wherein alkyl, phenyl, heteroaryl, heterocycloalkyl, and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from halogen, C₁₋₄ alkyl, hydroxy, 15 and C₁₋₄ alkoxy, or two R⁹ groups together with the atom to which they are attached form a 4- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC₁₋₄ alkyl;

r is 1 or 2;

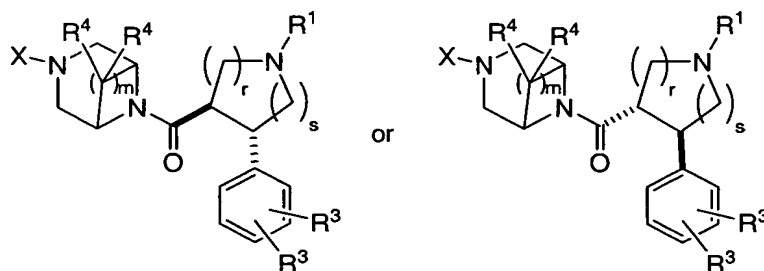
s is 0, 1 or 2;

20 m is 0, 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4; and

p is 0, 1, or 2.

15. The compound of Claim 1 of the following structural formula with the 25 indicated *trans* relative stereochemical configuration:



or a pharmaceutically acceptable salt thereof;

wherein

X is selected from the group consisting of

- (1) $-(CH_2)_{0-1}$ -phenyl,
- (2) $-(CH_2)_{0-1}$ -heteroaryl, and
- (3) $-(CH_2)_{0-1}C(R^5)(R^6)(R^7)$,

5 wherein phenyl and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3 , and wherein any methylene (CH_2) in X is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C_{1-4} alkyl;

10 R^1 is selected from the group consisting of hydrogen, C_{1-4} alkyl, and $-(CH_2)_{0-1}$ phenyl;

each R^3 is independently selected from the group consisting of

- (1) C_{1-8} alkyl,
- 15 (2) C_{2-8} alkenyl,
- (3) $-(CH_2)_{0-1}$ -phenyl,
- (4) $-(CH_2)_{0-1}$ -naphthyl,
- (5) $-(CH_2)_{0-1}$ -heteroaryl,
- (6) $-(CH_2)_{0-1}$ - C_{2-7} heterocycloalkyl,
- 20 (7) $-(CH_2)_{0-1}$ - C_{3-7} cycloalkyl,
- (8) halogen,
- (9) OR^9 ,
- (10) $-(CH_2)_{0-1}-C(O)R^9$,
- (11) $-(CH_2)_{0-1}-OC(O)R^9$,
- 25 (12) $-(CH_2)_{0-1}-C(O)OR^9$,
- (13) $-(CH_2)_{0-1}-C\equiv N$,
- (14) NO_2 ,
- (15) $-(CH_2)_{0-1}-N(R^9)_2$,
- (16) $-(CH_2)_{0-1}-C(O)N(R^9)_2$,
- 30 (17) $-(CH_2)_{0-1}-NR^9C(O)R^9$,
- (18) $-(CH_2)_{0-1}-NR^9C(O)OR^9$,
- (19) $-(CH_2)_{0-1}NR^9C(O)$ -heteroaryl,
- (20) $-(CH_2)_{0-1}NR^9C(O)N(R^9)_2$,
- (21) $-(CH_2)_{0-1}C(O)NR^9N(R^9)_2$,
- 35 (22) $-(CH_2)_{0-1}-C(O)NR^9NR^9C(O)R^9$,

(23) $-(\text{CH}_2)_{0-1}-\text{NR}^9\text{S}(\text{O})_{1-2}\text{R}^9$,

(24) $-(\text{CH}_2)_{0-1}-\text{S}(\text{O})_{1-2}\text{N}(\text{R}^9)_2$,

(25) $-(\text{CH}_2)_{0-1}-\text{S}(\text{O})_{0-2}\text{R}^9$,

(26) $\text{O}(\text{CH}_2)_{0-1}-\text{C}(\text{O})\text{N}(\text{R}^9)_2$,

(27) CF_3 ,

(28) CH_2CF_3 ,

(29) OCF_3 , and

(30) OCH_2CF_3 ,

wherein alkenyl, phenyl, naphthyl, heteroaryl are unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, C_{1-4} alkyl, trifluoromethyl, and C_{1-4} alkoxy, and wherein any alkyl, cycloalkyl, heterocycloalkyl, and methylene (CH_2) carbon atom in R^3 is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, oxo, C_{1-4} alkyl, trifluoromethyl, and C_{1-4} alkoxy, or two R^3 substituents on the same carbon atom are taken together with the carbon atom to form a cyclopropyl group;

each R^4 is independently selected from the group consisting of

(1) hydrogen,

(2) C_{1-8} alkyl,

(3) $-(\text{CH}_2)_{0-1}-\text{C}_{3-6}$ cycloalkyl,

(4) $-(\text{CH}_2)_{0-1}$ -aryl,

(5) hydroxy,

(6) halogen, and

(7) amino;

R^5 is independently selected from the group consisting of

(1) hydrogen,

(2) C_{1-8} alkyl,

(3) C_{2-8} alkenyl,

(4) C_{2-8} alkynyl,

(5) C_{1-8} alkoxy,

(6) $-(\text{CH}_2)_{0-1}-\text{C}_{3-7}$ cycloalkyl,

(7) $-(\text{CH}_2)_{0-1}-\text{C}_{2-7}$ heterocycloalkyl,

(8) $-(\text{CH}_2)_{0-1}$ -phenyl,

(9) $-(\text{CH}_2)_{0-1}$ -naphthyl,

(10) $-(\text{CH}_2)_{0-1}$ -heteroaryl, and

(11) $-(\text{CH}_2)_{0-1}\text{-C}_{3-7}$ bicycloalkyl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3 , and alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from R^3 and oxo, and wherein any methylene (CH_2) in R^5 is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C_{1-4} alkyl;

R^6 is selected from the group consisting of

- (1) hydrogen, and
- (2) C_{1-8} alkyl;

R^7 is selected from the group consisting of

- (1) $-(\text{CH}_2)_{0-3}\text{-N}(\text{R}^8)_2$,
- (2) $-(\text{CH}_2)_{0-3}\text{-NR}^8\text{C}(\text{O})\text{R}^8$,
- (3) $-(\text{CH}_2)_{0-3}\text{-NR}^8\text{C}(\text{O})\text{OR}^8$,
- (4) $-(\text{CH}_2)_{0-3}\text{-NR}^8\text{C}(\text{O})\text{N}(\text{R}^8)_2$,
- (5) $-(\text{CH}_2)_{0-3}\text{-NR}^8\text{S}(\text{O})\text{R}^8$,
- (6) $-(\text{CH}_2)_{0-3}\text{-NR}^8\text{S}(\text{O})_2\text{R}^8$, and
- (7) $-(\text{CH}_2)_{0-3}\text{-NR}^8\text{S}(\text{O})_2\text{N}(\text{R}^8)_2$,

wherein any methylene (CH_2) in R^7 is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C_{1-4} alkyl, or two R^8 substituents together with the carbon, nitrogen or sulfur atom to which they are attached form a 5, 6, or 7-membered saturated or unsaturated nitrogen containing ring optionally substituted with one to three groups independently selected from C_{1-8} alkyl and oxo;

each R^8 is independently selected from the group consisting of

- (1) hydrogen,
- (2) C_{1-8} alkyl,
- (3) C_{2-8} alkenyl,
- (4) $-(\text{CH}_2)_{0-1}\text{-C}_{3-7}$ cycloalkyl,
- (5) $-(\text{CH}_2)_{0-1}\text{-C}_{2-7}$ heterocycloalkyl,
- (6) $-(\text{CH}_2)_{0-1}\text{-C}_{3-7}$ bicycloalkyl,
- (7) $-(\text{CH}_2)_{0-1}\text{-phenyl}$,
- (8) $-(\text{CH}_2)_{0-1}\text{-naphthyl}$, and

(9) $-(CH_2)_{0-1}$ -heteroaryl,

wherein alkyl, alkenyl, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from R^3 and oxo, and wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3 , and wherein any methylene (CH_2) in R^8 is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C_{1-4} alkyl, or two R^8 groups together with the atom to which they are attached form a 5- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and $-NC_{1-4}$ alkyl;

each R^9 is independently selected from the group consisting of

- (1) hydrogen,
- (2) C_{1-8} alkyl,
- (3) phenyl,
- (4) heteroaryl,
- (5) $-(CH_2)_{0-1}$ heterocycloalkyl, and
- (6) C_{3-6} cycloalkyl,

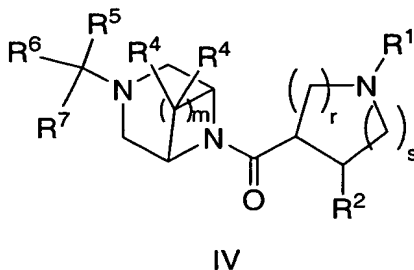
wherein alkyl, phenyl, heteroaryl, heterocycloalkyl, and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from halogen, C_{1-4} alkyl, hydroxy, and C_{1-4} alkoxy, or two R^9 groups together with the atom to which they are attached form a 4- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and $-NC_{1-4}$ alkyl;

r is 1 or 2;

s is 0, 1 or 2; and

m is 0, 1, 2, 3 or 4.

16. A compound of structural formula IV:



or a pharmaceutically acceptable salt thereof;
wherein

R¹ is selected from the group consisting of

- 5 (1) hydrogen,
- (2) amidino,
- (3) C₁₋₄ alkyliminoyl,
- (4) C₁₋₁₀ alkyl,
- (5) -(CH₂)_n-C₃₋₇ cycloalkyl,
- 10 (6) -(CH₂)_n-phenyl,
- (7) -(CH₂)_n-naphthyl, and

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R³, and alkyl and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from R³ and oxo;

R² is selected from the group consisting of

- (1) phenyl,
- (2) naphthyl, and
- (3) heteroaryl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R³;

each R³ is independently selected from the group consisting of

- (1) C₁₋₈ alkyl,
- 25 (2) C₂₋₈ alkenyl,
- (3) -(CH₂)_n-phenyl,
- (4) -(CH₂)_n-naphthyl,
- (5) -(CH₂)_n-heteroaryl,
- (6) -(CH₂)_n-C₂₋₇ heterocycloalkyl,
- 30 (7) -(CH₂)_n-C₃₋₇ cycloalkyl,
- (8) halogen,
- (9) OR⁹,
- (10) -(CH₂)_n-C(O)R⁹,
- (11) -(CH₂)_n-OC(O)R⁹,
- 35 (12) -(CH₂)_n-C(O)OR⁹,

- (13) $-(CH_2)_n C \equiv N$,
 (14) NO_2 ,
 (15) $-(CH_2)_n N(R^9)_2$,
 (16) $-(CH_2)_n C(O)N(R^9)_2$,
 5 (17) $-(CH_2)_n NR^9C(O)R^9$,
 (18) $-(CH_2)_n NR^9C(O)OR^9$,
 (19) $-(CH_2)_n NR^9C(O)$ -heteroaryl,
 (20) $-(CH_2)_n NR^9C(O)N(R^9)_2$,
 (21) $-(CH_2)_n C(O)NR^9N(R^9)_2$,
 10 (22) $-(CH_2)_n C(O)NR^9NR^9C(O)R^9$,
 (23) $-(CH_2)_n NR^9S(O)_p R^9$,
 (24) $-(CH_2)_n S(O)_p N(R^9)_2$,
 (25) $-(CH_2)_n S(O)_p R^9$,
 (26) $O(CH_2)_n C(O)N(R^9)_2$,
 15 (27) CF_3 ,
 (28) CH_2CF_3 ,
 (29) OCF_3 , and
 (30) OCH_2CF_3 ,

wherein alkenyl, phenyl, naphthyl, heteroaryl are unsubstituted or substituted with one to three
 20 substituents independently selected from halogen, hydroxy, C₁₋₄ alkyl, trifluoromethyl, and C₁₋₄
 alkoxy, and wherein any alkyl, cycloalkyl, heterocycloalkyl, and methylene (CH₂) carbon atom
 in R³ is unsubstituted or substituted with one to two groups independently selected from
 halogen, hydroxy, oxo, C₁₋₄ alkyl, trifluoromethyl, and C₁₋₄ alkoxy, or two R³ substituents on
 the same carbon atom are taken together with the carbon atom to form a cyclopropyl group;

25 each R⁴ is independently selected from the group consisting of

- (1) hydrogen,
 (2) C₁₋₈ alkyl,
 (3) $-(CH_2)_n C_{3-6}$ cycloalkyl,
 30 (4) $-(CH_2)_n$ -aryl,
 (5) hydroxy,
 (6) halogen, and
 (7) amino;

35 R⁵ is independently selected from the group consisting of

- (1) hydrogen,
 (2) C₁₋₈ alkyl,
 (3) C₂₋₈ alkenyl,
 (4) C₂₋₈ alkynyl,
 5 (5) C₁₋₈ alkoxy,
 (6) -(CH₂)_nC₃₋₇ cycloalkyl,
 (7) -(CH₂)_nC₂₋₇ heterocycloalkyl,
 (8) -(CH₂)_n-phenyl,
 (9) -(CH₂)_n-naphthyl,
 10 (10) -(CH₂)_n-heteroaryl, and
 (11) -(CH₂)_nC₃₋₇ bicycloalkyl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R³, and alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups
 15 independently selected from R³ and oxo, and wherein any methylene (CH₂) in R⁵ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl;

R⁶ is selected from the group consisting of

- 20 (1) hydrogen, and
 (2) C₁₋₈ alkyl;

R⁷ is selected from the group consisting of

- (1) -(CH₂)_nN(R⁸)₂,
 25 (2) -(CH₂)_nNR⁸C(O)R⁸,
 (3) -(CH₂)_nNR⁸C(O)OR⁸,
 (4) -(CH₂)_nNR⁸C(O)N(R⁸)₂,
 (5) -(CH₂)_nNR⁸S(O)R⁸,
 (6) -(CH₂)_nNR⁸S(O)₂R⁸, and
 30 (7) -(CH₂)_nNR⁸S(O)₂N(R⁸)₂,

wherein any methylene (CH₂) in R⁷ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl, or two R⁸ substituents together with the carbon, nitrogen or sulfur atom to which they are attached form a 5, 6, or 7-membered saturated or unsaturated nitrogen containing ring optionally substituted with one to three groups
 35 independently selected from C₁₋₈ alkyl and oxo;

each R⁸ is independently selected from the group consisting of

- (1) hydrogen,
- (2) C₁₋₈ alkyl,
- 5 (3) C₂₋₈ alkenyl,
- (4) -(CH₂)_nC₃₋₇ cycloalkyl,
- (5) -(CH₂)_nC₂₋₇ heterocycloalkyl,
- (6) -(CH₂)_nC₃₋₇ bicycloalkyl,
- (7) -(CH₂)_n-phenyl,
- 10 (8) -(CH₂)_n-naphthyl, and
- (9) -(CH₂)_n-heteroaryl,

wherein alkyl, alkenyl, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from R³ and oxo, and wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R³, and wherein any methylene (CH₂) in R⁸ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl, or two R⁸ groups together with the atom to which they are attached form a 5- to 8-

20

each R⁹ is independently selected from the group consisting of

- (1) hydrogen,
- (2) C₁₋₈ alkyl,
- (3) phenyl,
- 25 (4) heteroaryl,
- (5) -(CH₂)_n heterocycloalkyl, and
- (6) C₃₋₆ cycloalkyl,

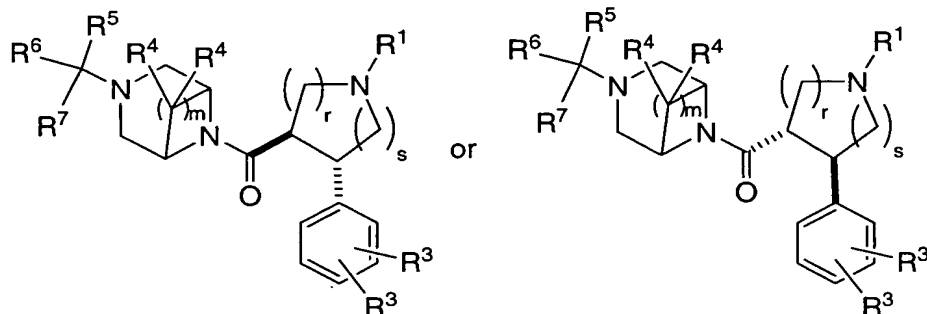
wherein alkyl, phenyl, heteroaryl, heterocycloalkyl, and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from halogen, C₁₋₄ alkyl, hydroxy, and C₁₋₄ alkoxy, or two R⁹ groups together with the atom to which they are attached form a 4- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC₁₋₄ alkyl;

r is 1 or 2;
 s is 0, 1 or 2;
 35 m is 0, 1, 2, 3, or 4;

n is 0, 1, 2, 3, or 4; and

p is 0, 1, or 2.

17. The compound of Claim 1 of the following structural formula with the indicated *trans* relative stereochemical configuration:



or a pharmaceutically acceptable salt thereof;

wherein

10 R^1 is selected from the group consisting of hydrogen, C_{1-4} alkyl, and $-(CH_2)_{0-1}$ phenyl;

each R^3 is independently selected from the group consisting of

- (1) C_{1-8} alkyl,
- 15 (2) C_{2-8} alkenyl,
- (3) $-(CH_2)_{0-1}$ -phenyl,
- (4) $-(CH_2)_{0-1}$ -naphthyl,
- (5) $-(CH_2)_{0-1}$ -heteroaryl,
- (6) $-(CH_2)_{0-1}$ - C_{2-7} heterocycloalkyl,
- 20 (7) $-(CH_2)_{0-1}$ - C_{3-7} cycloalkyl,
- (8) halogen,
- (9) OR^9 ,
- (10) $-(CH_2)_{0-1}-C(O)R^9$,
- (11) $-(CH_2)_{0-1}-OC(O)R^9$,
- 25 (12) $-(CH_2)_{0-1}-C(O)OR^9$,
- (13) $-(CH_2)_{0-1}-C\equiv N$,
- (14) NO_2 ,
- (15) $-(CH_2)_{0-1}-N(R^9)_2$,

- (16) $-(CH_2)_{0-1}-C(O)N(R^9)_2$,
 (17) $-(CH_2)_{0-1}-NR^9C(O)R^9$,
 (18) $-(CH_2)_{0-1}-NR^9C(O)OR^9$,
 (19) $-(CH_2)_{0-1}NR^9C(O)$ -heteroaryl,
 5 (20) $-(CH_2)_{0-1}NR^9C(O)N(R^9)_2$,
 (21) $-(CH_2)_{0-1}C(O)NR^9N(R^9)_2$,
 (22) $-(CH_2)_{0-1}-C(O)NR^9NR^9C(O)R^9$,
 (23) $-(CH_2)_{0-1}-NR^9S(O)_{1-2}R^9$,
 (24) $-(CH_2)_{0-1}-S(O)_{1-2}N(R^9)_2$,
 10 (25) $-(CH_2)_{0-1}-S(O)_{0-2}R^9$,
 (26) $O(CH_2)_{0-1}-C(O)N(R^9)_2$,
 (27) CF_3 ,
 (28) CH_2CF_3 ,
 (29) OCF_3 , and
 15 (30) OCH_2CF_3 ,

wherein alkenyl, phenyl, naphthyl, heteroaryl are unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, C₁₋₄ alkyl, trifluoromethyl, and C₁₋₄ alkoxy, and wherein any alkyl, cycloalkyl, heterocycloalkyl, and methylene (CH₂) carbon atom in R³ is unsubstituted or substituted with one to two groups independently selected from
 20 halogen, hydroxy, oxo, C₁₋₄ alkyl, trifluoromethyl, and C₁₋₄ alkoxy, or two R³ substituents on the same carbon atom are taken together with the carbon atom to form a cyclopropyl group;

each R⁴ is independently selected from the group consisting of

- 25 (1) hydrogen,
 (2) C₁₋₈ alkyl,
 (3) $-(CH_2)_{0-1}-C_{3-6}$ cycloalkyl,
 (4) $-(CH_2)_{0-1}$ -aryl,
 (5) hydroxy,
 (6) halogen, and
 30 (7) amino;

R⁵ is independently selected from the group consisting of

- (1) hydrogen,
 (2) C₁₋₈ alkyl,
 35 (3) C₂₋₈ alkenyl,

- (4) C₂₋₈ alkynyl,
- (5) C₁₋₈ alkoxy,
- (6) -(CH₂)₀₋₁-C₃₋₇ cycloalkyl,
- (7) -(CH₂)₀₋₁-C₂₋₇ heterocycloalkyl,
- 5 (8) -(CH₂)₀₋₁-phenyl,
- (9) -(CH₂)₀₋₁-naphthyl,
- (10) -(CH₂)₀₋₁-heteroaryl, and
- (11) -(CH₂)₀₋₁-C₃₋₇ bicycloalkyl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three
 10 groups independently selected from R³, and alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from R³ and oxo, and wherein any methylene (CH₂) in R⁵ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl;

15 R⁶ is selected from the group consisting of

- (1) hydrogen, and
- (2) C₁₋₈ alkyl;

20 R⁷ is selected from the group consisting of

- (1) -(CH₂)₀₋₃-N(R⁸)₂,
- (2) -(CH₂)₀₋₃-NR⁸C(O)R⁸,
- (3) -(CH₂)₀₋₃-NR⁸C(O)OR⁸,
- (4) -(CH₂)₀₋₃-NR⁸C(O)N(R⁸)₂,
- 25 (5) -(CH₂)₀₋₃-NR⁸S(O)R⁸,
- (6) -(CH₂)₀₋₃-NR⁸S(O)₂R⁸, and
- (7) -(CH₂)₀₋₃-NR⁸S(O)₂N(R⁸)₂,

wherein any methylene (CH₂) in R⁷ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl, or two R⁸ substituents together
 30 with the carbon, nitrogen or sulfur atom to which they are attached form a 5, 6, or 7-membered saturated or unsaturated nitrogen containing ring optionally substituted with one to three groups independently selected from C₁₋₈ alkyl and oxo;

each R⁸ is independently selected from the group consisting of

- 35 (1) hydrogen,

- (2) C₁₋₈ alkyl,
- (3) C₂₋₈ alkenyl,
- (4) -(CH₂)₀₋₁-C₃₋₇ cycloalkyl,
- (5) -(CH₂)₀₋₁-C₂₋₇ heterocycloalkyl,
- 5 (6) -(CH₂)₀₋₁-C₃₋₇ bicycloalkyl,
- (7) -(CH₂)₀₋₁-phenyl,
- (8) -(CH₂)₀₋₁-naphthyl, and
- (9) -(CH₂)₀₋₁-heteroaryl,

10 wherein alkyl, alkenyl, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from R³ and oxo, and wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R³, and wherein any methylene (CH₂) in R⁸ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl, or two R⁸ groups together with the atom to which they are attached form a 5- to 8-
15 membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC₁₋₄ alkyl;

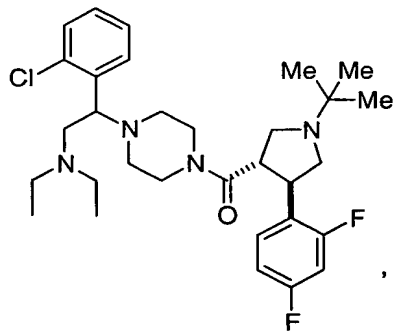
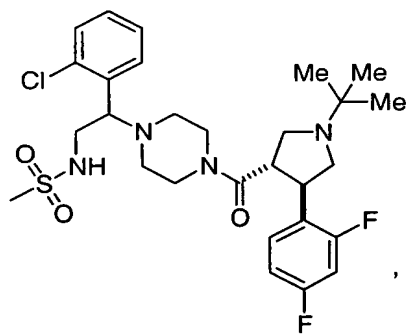
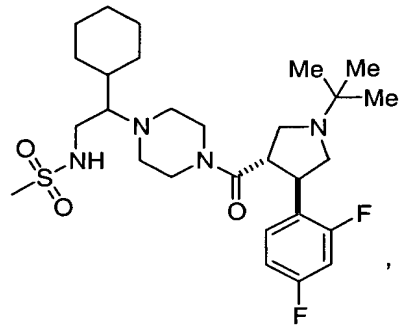
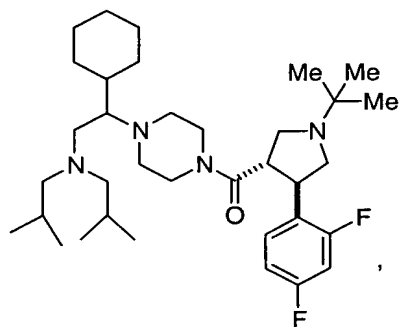
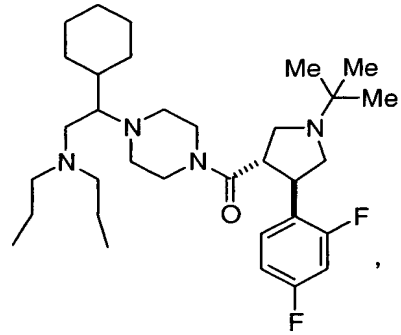
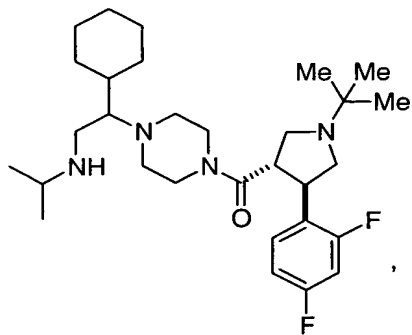
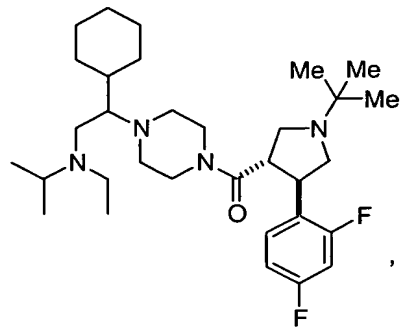
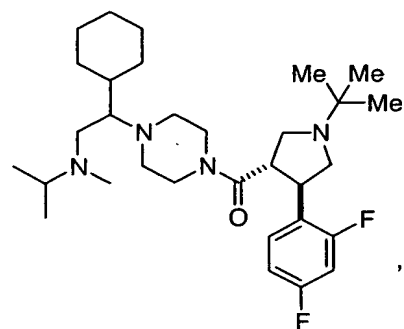
each R⁹ is independently selected from the group consisting of

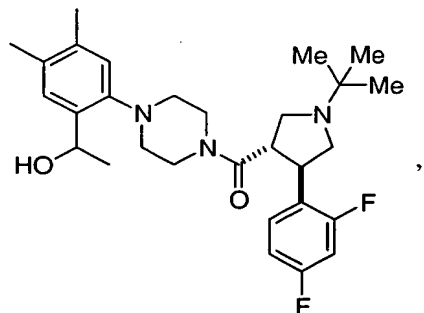
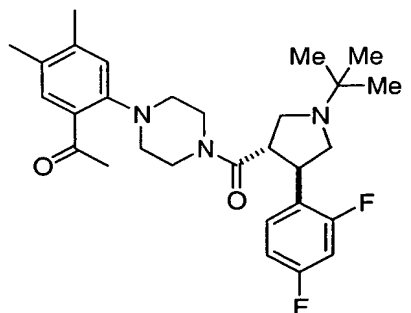
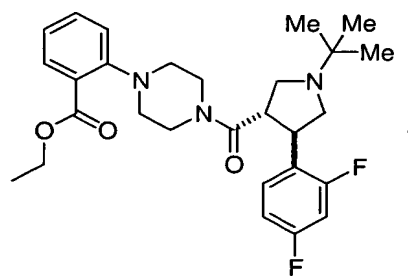
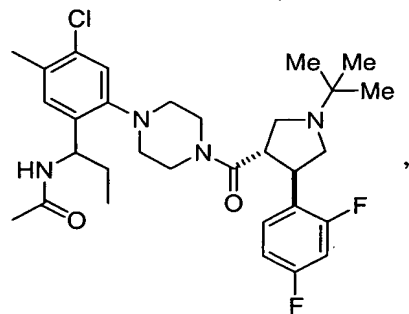
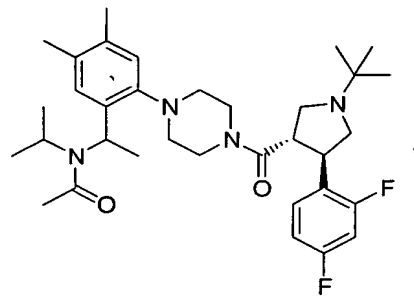
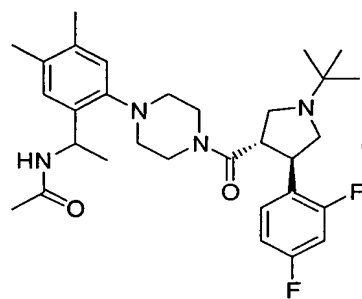
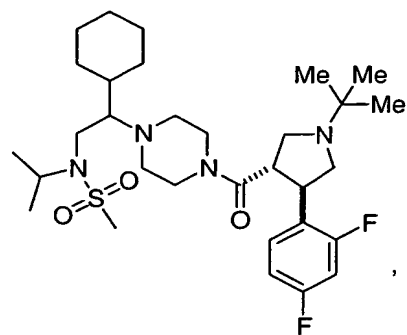
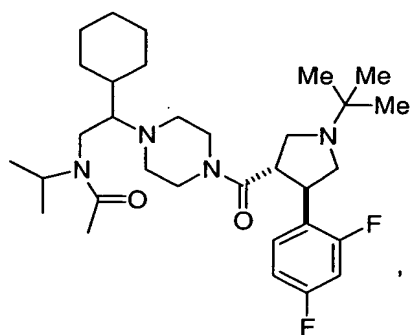
- (1) hydrogen,
- 20 (2) C₁₋₈ alkyl,
- (3) phenyl,
- (4) heteroaryl,
- (5) -(CH₂)₀₋₁ heterocycloalkyl, and
- (6) C₃₋₆ cycloalkyl,

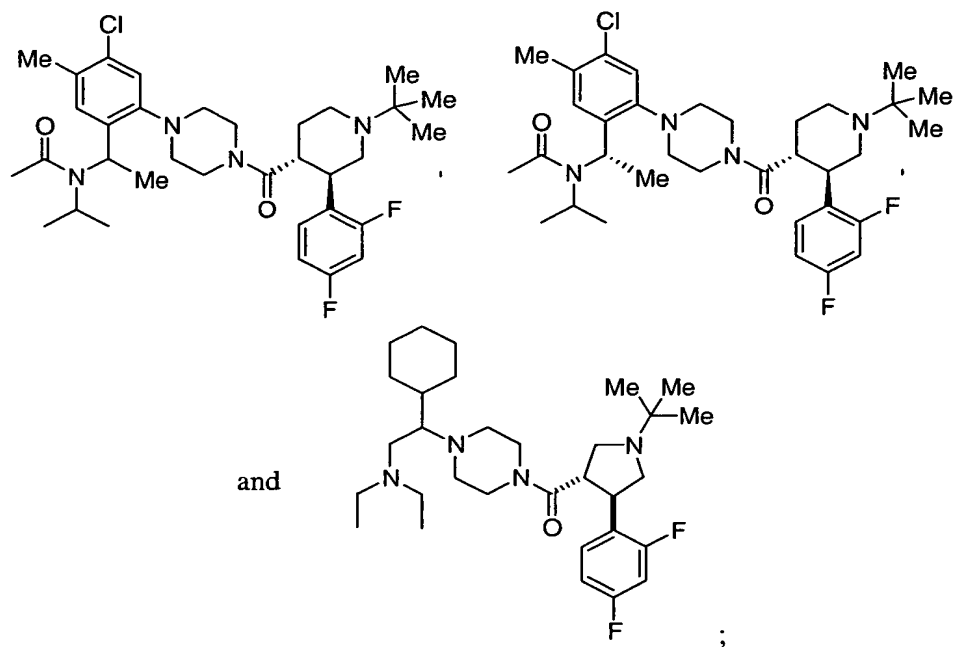
25 wherein alkyl, phenyl, heteroaryl, heterocycloalkyl, and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from halogen, C₁₋₄ alkyl, hydroxy, and C₁₋₄ alkoxy, or two R⁹ groups together with the atom to which they are attached form a 4- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC₁₋₄ alkyl;

30 r is 1 or 2;
s is 0, 1 or 2; and
m is 0, 1, 2, 3 or 4.

18. The compound of Claim 1 selected from the group consisting of:

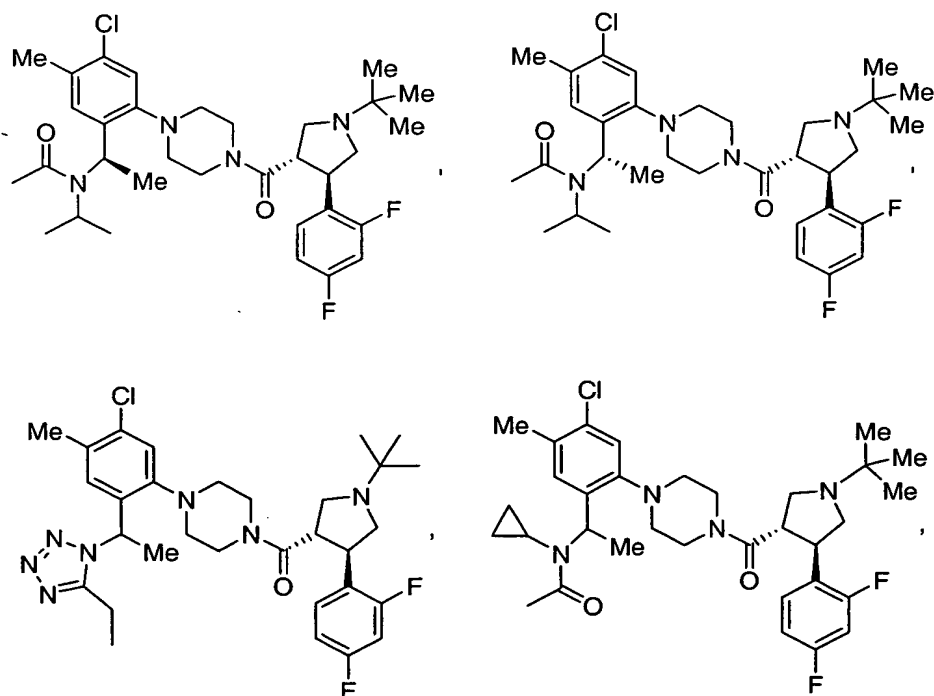


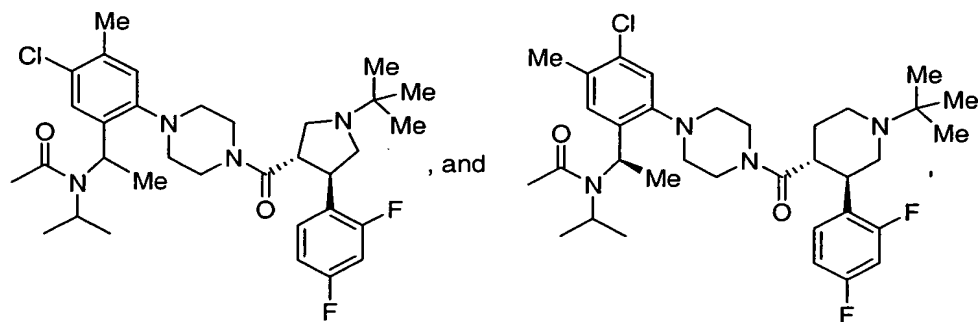




or a pharmaceutically acceptable salt thereof.

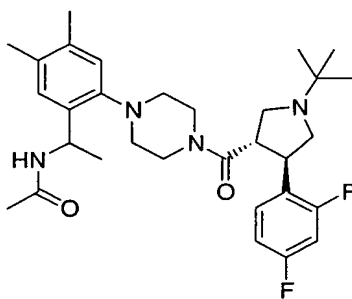
- 5 19. The compound of Claim 1 selected from the group consisting of:





or a pharmaceutically acceptable salt thereof.

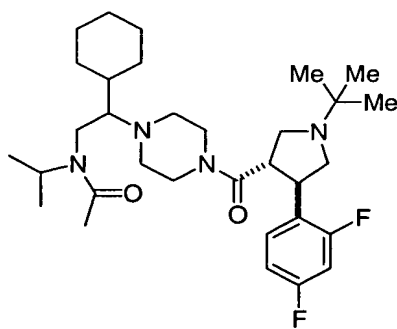
20. The compound of Claim 18 which is:



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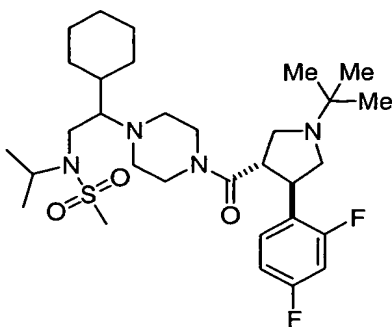
or a pharmaceutically acceptable salt thereof.

21. The compound of Claim 18 which is:



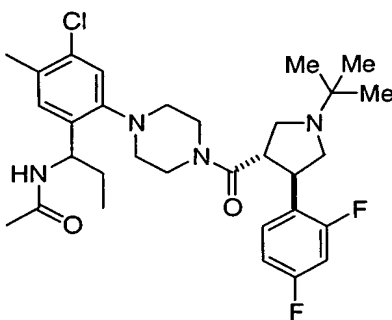
10 or a pharmaceutically acceptable salt thereof.

22. The compound of Claim 18 which is:



or a pharmaceutically acceptable salt thereof.

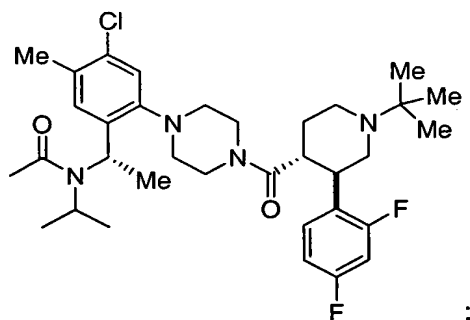
23. The compound of Claim 18 which is:



5

or a pharmaceutically acceptable salt thereof.

24. The compound of Claim 18 which is:



;

10 or a pharmaceutically acceptable salt thereof.

25. A method for the treatment or prevention of disorders, diseases or conditions responsive to the activation of the melanocortin-4 receptor in a mammal in need

thereof which comprises administering to the mammal a therapeutically or prophylactically effective amount of a compound according to Claim 1.

26. A method for the treatment or prevention of obesity in a mammal in need thereof which comprises administering to the mammal a therapeutically or prophylactically effective amount of a compound according to Claim 1.

27. A method for the treatment or prevention of diabetes mellitus in a mammal in need thereof comprising administering to the mammal a therapeutically or prophylactically effective amount of a compound according to Claim 1.

28. A method for the treatment or prevention of male or female sexual dysfunction in a mammal in need thereof comprising administering to the mammal a therapeutically or prophylactically effective amount of a compound according to Claim 1.

29. A method for the treatment or prevention of erectile dysfunction in a mammal in need thereof comprising administering to the mammal a therapeutically or prophylactically effective amount of a compound according to Claim 1.

30. A pharmaceutical composition which comprises a compound of Claim 1 and a pharmaceutically acceptable carrier.

31. The pharmaceutical composition of Claim 30 further comprising a second active ingredient selected from the group consisting of an insulin sensitizer, an insulin mimetic, a sulfonylurea, an α -glucosidase inhibitor, a HMG-CoA reductase inhibitor, a serotonergic agent, a β 3-adrenoreceptor agonist, a neuropeptide Y1 antagonist, a neuropeptide Y5 antagonist, a pancreatic lipase inhibitor, a cannabinoid CB1 receptor antagonist or inverse agonist, a melanin-concentrating hormone receptor antagonist, a bombesin receptor subtype 3 agonist, and a ghrelin receptor antagonist.

32. The pharmaceutical composition of Claim 30 further comprising a second active ingredient selected from the group consisting of a type V cyclic-GMP-selective phosphodiesterase inhibitor, an α 2-adrenergic receptor antagonist, and a dopaminergic agent.

33. A method of treating erectile dysfunction in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of the composition of Claim 30.

5 34. A method of treating erectile dysfunction in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with a type V cyclic-GMP-selective phosphodiesterase inhibitor, an α_2 -adrenergic receptor antagonist, or a dopaminergic agent.

10 35. A method of treating diabetes in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of the composition of Claim 30.

36. A method of treating obesity in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of the composition of Claim 30.

15 37. A method of treating diabetes or obesity in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with an insulin sensitizer, an insulin mimetic, a sulfonylurea, an α -glucosidase inhibitor, a HMG-CoA reductase inhibitor, a serotonergic agent, a β_3 -adrenoreceptor agonist, a neuropeptide Y1 antagonist, a neuropeptide Y5 antagonist, a pancreatic lipase inhibitor, a cannabinoid CB₁ receptor antagonist or inverse agonist, a melanin-concentrating hormone receptor antagonist, a bombesin receptor subtype 3 agonist, or a ghrelin receptor antagonist.

25 38. The compound of Claim 1 wherein the pharmaceutically acceptable salt thereof is the hydrochloride salt.

39. The compound of Claim 1 wherein the pharmaceutically acceptable salt thereof is the trifluoroacetic acid salt.

30 40. The compound of Claim 1 wherein the pharmaceutically acceptable salt thereof is the bis phosphate salt.

41. The use of a compound according to Claim 1 for the manufacture of a medicament useful for the treatment of a disease mediated by the melanocortin-4 receptor in a human subject in need thereof.

5 42. The use according to Claim 41 wherein the disease mediated by the melanocortin-4 receptor is selected from the group consisting of obesity, diabetes, male sexual dysfunction and female sexual dysfunction.

10 43. The use according to Claim 42, wherein the male sexual dysfunction is male erectile dysfunction.

15 44. The use of a compound according to Claim 1 for the manufacture of a medicament useful for the prevention of a disease mediated by the melanocortin-4 receptor in a human subject at risk therefor.

45. The use according to Claim 44 wherein the disease mediated by the melanocortin-4 receptor is selected from the group consisting of obesity, diabetes, male sexual dysfunction and female sexual dysfunction.

20 46. The use according to Claim 45, wherein the male sexual dysfunction is male erectile dysfunction.